

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Tessier-Lavigne et al.

Group Art Unit: 1631

Serial No. 09/273,098

Examiner: Allen, M.

Filed: March 19, 1999

Attorney Docket No. UC99-244-2

For: *Compositions for Promoting Nerve
Regeneration*

DECLARATION UNDER 37CFR1.132

I, Corey S. Goodman, declare and state as follows:

1. I am a Professor in the Department of Molecular and Cell Biology at the University of California, Berkeley, an investigator in the Howard Hughes Medical Institute, and the Director of the Wills Neuroscience Institute. The Regents of the University of California is the assignee of the subject patent application. I am knowledgeable and experienced in the field of nerve cell guidance and head one of the world's leading research teams in this field. I have read and am familiar with the contents of the above application and the cited Artavanis-Tsakonas et al. and Goodman et al. patents.

2. Natural sequence Slit-N polypeptides are known in the art to refer to a class of proteins naturally produced as N-terminal proteolytic fragments of Slit polypeptides. Natural sequence Slit-N polypeptides are naturally occurring N-terminal proteolytic fragments of Slit proteins which stimulate elongation and branching of neuronal axons. Residue boundaries of natural sequence Slit-N polypeptides are readily determined (see, p.6, lines 2-29) and exemplified in the application, e.g. hSlit-2-N is bound by Met1 and Arg1117 of hSlit-2; dSlit-2-N is bound by Met1 and Gln1111 of dSlit (see, p.3, lines 26-27).

Furthermore, Slit proteins are an art recognized class of neuroactive proteins and diverse and numerous examples of Slit proteins were known as of March 19, 1999. For example, Brose et al. (1999) describes human (h) Slit polypeptides: hSlit-1, hSlit-2, hSlit-3; rat (r) Slit polypeptides: rSlit-1, rSlit-2, rSlit-3; as well as Slit polypeptides from *Drosophila* and *C. elegans*. See Brose at p.796. In fact, many of these proteins were initially characterized in my laboratory.

3. The cited Artavanis-Tsakonas patent describes a human Notch protein. Like human Slit proteins, human notch is well-known. Human notch is known to be structurally and functionally

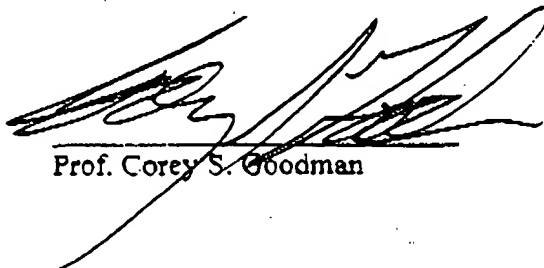
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unrelated to Slit and Slit-N polypeptides. Not only is this fact well known in the art but it is readily confirmed by simply comparing the known disparate sequences of these proteins.

Goodman et al. (US Patent No.6,046,015) describes and claims slit fragments generally, but there is no mention or suggestion of natural sequence Slit-N polypeptides. Prior to this application, the art taught that Slit proteins were chemorepellents. To my knowledge, there is no prior art suggestion of the finding that these polypeptides "function as positive regulators of axon collateral formation during the establishment or remodeling of neural circuits and that the activity of these proteins can synergize in vitro and in vivo with other neurotrophic agents like NGF..."

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application and any patent issuing therefrom.

Date: February 20, 2001



Prof. Corey S. Goodman

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